ORIGINAL ARTICLE

AG-2020-250
doi.org/10.1590/S0004-2803.202100000-55

Comparative analysis of two oral contrast agent volumes for computed tomography enterography in Crohn's disease patients

Fernanda Lofiego **RENOSTO**[1], Jaqueline Ribeiro de **BARROS**[1], Guilherme A **BERTOLDI**[2,3], Sergio Ribeiro **MARRONE**[4], Ligia Yukie **SASSAKI**[1] and Rogerio **SAAD-HOSSNE**[5]

Received: 5 December 2020
Accepted: 3 May 2021

ABSTRACT – **Background** – Crohn's disease (CD) is an inflammatory bowel disease characterized by a chronic and recurrent inflammation of the gastrointestinal tract caused by an interaction of genetic and environmental factors. **Objective** – To compare the quality and acceptance of two different oral contrast volumes for computed tomography enterography in Crohn's disease patients. **Methods** – A cross-sectional study was conducted in 58 consecutive Crohn's disease patients who randomly received an oral contrast agent composed of 78.75 g polyethylene glycol diluted in either 1,000 mL or 2,000 mL of water. An examination was performed to evaluate the presence of inflammation or complications in the small bowel. The variables included the quality of intestinal segment filling and luminal distension, and oral contrast agent acceptance and tolerance in the patients. Statistical analysis included descriptive statistics and association tests. **Results** – A total of 58 patients were assessed, in which 58.6% were female, 34.5% exhibited clinically-active disease, and 63.8% were receiving biologic therapy. As for comparative analysis between the two different volumes of oral contrast, no statistically significant difference was found regarding bowel loop filling (P=0.58) and adequate luminal distension (P=0.45). Patients who received a larger volume (2,000 mL) exhibited side-effects more frequently (51.7% vs 31.0%; P=0.06) and had greater difficulty ingesting the agent (65.5% vs 37.9%; P=0.07) compared with a volume of 1,000 mL. **Conclusion** – The quality of computed tomography enterography was not influenced by the contrast volume. However, acceptance and tolerance were better in the 1,000 mL group.

Keywords – Contrast agent, Crohn's disease, polyethylene glycol, tomography.

INTRODUCTION

Crohn's disease (CD) is an inflammatory bowel disease characterized by a chronic and recurrent inflammation of the gastrointestinal tract caused by an interaction of genetic and environmental factors[1,2]. Symptoms are heterogeneous, but commonly include abdominal pain, weight loss and chronic diarrhea[2]. Systemic symptoms, such as fatigue, anorexia and fever, may also occur[2].

Radiological exams play a fundamental role in the treatment of CD patients and can be used during diagnostic investigation to determine the extent of the disease, detect complications, evaluate inflammatory activity and assess the response to medical therapy[3]. Computed tomography (CT) enterography is a variation of CT that allows for the evaluation of each bowel segment individually, without overlapping loops[4]. The degree of bowel wall thickening can be assessed, as well as characteristics of the mesentery and perimesenteric fat[5]. Furthermore, the presence of fistulas and fistulous tracts, abscesses, dilations and stenoses can be detected[6]. Finally, and most importantly, the degree of inflammatory activity of CD can be determined[7]. However, in order to carry out the exam and for its correct analysis, an intestinal contrast agent must be ingested via the oral route in an adequate manner.

The enteric contrast agent must not only enable the detection of bowel wall changes, but also ensure optimal luminal distension, which differs from the requirements of conventional CT[8]. The main contrast agents are positive, such as barium sulfate and iodine, and neutral, such as water, water with methylcellulose, barium with sorbitol, milk, polyethylene glycol (PEG), or VoLumen[9]. PEG exhibits good action in the gut, good acceptance by patients and lower side-effect indices[10,11].

Studies are diverse regarding the best contrast agent and the ideal volume for adequate small bowel distension in CT enterography[12]. Thus, the objective of the present study was to compare the quality and acceptance of two different volumes of PEG-based oral contrast for CT enterography among CD patients.

METHODS

Study design and patient selection

A cross-sectional observational study of 62 CD patients submitted to CT enterography was conducted. The sample size was based on the number of CD patients attending our service. All patients who underwent examination at the time of collection were invited to participate in the study. The collection period was

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received
Research performed at: São Paulo State University (UNESP), Medical School, Department of Internal Medicine, Botucatu, SP, Brazil.
[1] Universidade Estadual Paulista, Faculdade de Medicina, Departamento de Clínica Médica, Botucatu, SP, Brasil. [2] Hospital Erasto Gaertner, Curitiba, PR, Brasil. [3] Hospital Pequeno Príncipe, Curitiba, PR, Brasil. [4] Universidade Estadual Paulista, Faculdade de Medicina, Departamento de Radiologia, Botucatu, SP, Brasil. [5] Universidade Estadual Paulista, Faculdade de Medicina, Departamento de Cirurgia, Botucatu, SP, Brasil.
Corresponding author: Fernanda Renosto. E-mail: fernandalofiegorenosto@gmail.com

from January 2015 to July 2016. The intention of the exam was to assess the inflammatory process or the presence of complications, such as stenosis, abscess or fistula located in the small bowel. Inclusion criteria included confirmed CD according to clinical, endoscopic and radiographic parameters, and an age above 18 years. Exclusion criteria were an inability to ingest the contrast agent via the oral route, creatinine >1.5 mg/dL, presence of chronic renal failure, pregnancy, or allergy to the ionic contrast or to PEG. The study was approved by the Research Ethics Committee of Botucatu Medical School, São Paulo State University (CAAE: 34584114.5.0000.5411), Brazil, and a written informed consent was signed by all subjects before inclusion.

Clinical assessment (performed by a gastroenterologist)

The Crohn's Disease Activity Index (CDAI) was used to assess the disease activity in patients[13]. The Montreal Classification was used to classify the disease according to the age at diagnosis, disease location and presence of complications such as stenosis, fistula, or perianal disease[14].

Randomization and CT enterography protocol

Patients were consecutively divided into two groups that received different volumes of oral contrast agent. The agent consisted of 78.5 g PEG, which was diluted in either 1,000 mL or 2,000 mL of water. The total volume was ingested over 60 minutes in 15-minute intervals. Patients received 20 mg of scopolamine butylbromide intravenously 45 minutes after preparation. Examinations were performed using a 16-slice multidetector tomograph (Activion, Toshiba Medical Systems Corp., Tokyo, Japan). After preparation, imaging was performed by injecting intravenous non-ionic iodine contrast, varying between 1.5 mL and 2.0 mL/kg, not exceeding 150 mL, using a pump injector at a rate of 3.0 mL/s[15]. Images were acquired 60 seconds after contrast injection, beginning with slices above the diaphragm and ending at the pubic symphysis[16]. The following parameters were used: mA modulation 10–300, 120 kVp, volume 2 mm x 1 mm, rotation time 0.75 seconds, axial slice thickness 5 mm x 5 mm. After image acquisition, the volumes obtained of 2 mm x 1 mm slices were reconstructed in a coronal and sagittal maximum intensity projection (MIP), at 5 mm thickness and 3 mm intervals.

Evaluation of the quality of examination

Images were assessed by an experienced CD radiologist, blinded for the patient group. The following parameters were analyzed: a) adequate filling of bowel segments (jejunum, ileum, ascending colon, transverse colon, descending colon, and rectosigmoid); b) number of filled segments (1–6); c) luminal distension of the bowel (adequate ≥2 cm vs inadequate <2 cm)[17,18]; d) small bowel wall thickness (≤4 mm vs >4mm)[19]; e) presence of disease activity (jejunum, ileum, terminal ileum, appendix, ascending colon, transverse colon, descending colon, rectosigmoid); f) presence of complications (fistula, stenosis, intestinal obstruction, abscess, and intestinal dilation); g) presence of comb sign.

Adequate filling was based on the amount of oral contrast agent in the intestine. Adequate filling was considered when the number of filled segments was above four. Adequate small bowel distension requires an oral contrast agent, which should cause uniform intraluminal attenuation, highlighting the contrast between the luminal content and the bowel wall. Disease activity was based on the bowel wall thickness, presence of comb sign or the presence of complications. Intestinal obstruction was considered at a loop dilation diameter >2.5 cm, the presence of an air-fluid level, and disproportion regarding the distal loop segment[20]. Fistula was classified as internal fistula (enteroenteric, enterovesical, enterovaginal) or external fistula (enterocutaneous). Comb sign was defined as the presence of engorged vasa recta penetrating the bowel wall perpendicular to the lumen[21].

Evaluation of acceptance and tolerance of the contrast agent

Acceptance and tolerance of the contrast agent was assessed by a questionnaire, which inquired about the taste of the neutral oral contrast, ease of ingestion, total time of ingestion. The answers to these questions could be easy, moderate, difficult and very difficult. The presence of side effects such as nausea, vomiting, abdominal pain and malaise was evaluated and was classified according to its intensity in low, medium or high intensity. If the responses obtained were easy for ingestion, flavor, total time of ingestion, and absence or low frequency and intensity for side effects, the preparation was classified as good acceptance and good tolerance.

Laboratory examinations

C-reactive protein (CRP) value was used to assess disease inflammatory activity.

Statistical analysis

The population was submitted to a descriptive analysis by calculating the mean and standard deviation or median and quartiles for quantitative variables, and frequency and ratio for qualitative variables. Comparative analysis was performed by means of analysis of variance (ANOVA) or the Fisher's exact test when needed. Continuous variables were compared using ANOVA and a generalized linear model and gamma distribution. Statistical significance was set at $P<0.05$. Analyses were performed using SAS software for Windows, version 9.3.

RESULTS

A total of 62 patients were included in the study. Four were excluded for not fully completing the examination. Data from 58 patients were included in the final analysis, with 29 allocated to each group. Stricturing disease was most prevalent in the 2,000 mL group ($P=0.04$) (TABLE 1).

Strictures were diagnosed in 39.7% (n=23) of patients, dilation in 37.9% (n=22) (FIGURE1), comb sign in 27.6% (n=16), fistula in 22.4% (n=13) (FIGURE 2), and abscess in 13.78% (n=8) (FIGURE 3), showing no statistical difference among groups ($P>0.05$).

There was no statistical difference between the quality of examinations in the two different contrast agent volume groups. Adequate filling of the ileum was found in the majority of patients studied, with no difference between groups ($P=0.83$). Colon segments did not exhibit adequate filling, even in the 2,000 mL group (TABLE 2). There was no statistical difference in the number of filled segments between groups ($P=0.58$). Images of the quality of examinations and visualizations of the disease complications in the two different contrast agent volume groups can be seen in FIGURES 1 to 9.

In the comparative analysis of acceptance and tolerance, no difference was found between the different volumes of oral contrast agent. However, the presence of side effects was more frequent in

TABLE 1. Clinical characteristics of patients according to oral contrast agent volume.

	1,000 mL (n=29)	2,000 mL (n=29)	*P*
Age in years, mean (SD)	43.5±15.3	40.5±13.0	0.42
Gender female, n (%)	20 (69.0)	14 (48.3)	0.20
Montreal classification, n (%)			
Age at diagnosis			
A1: <17 years	5 (17.3)	2 (6.80)	
A2: between 17 and 40 years	15 (51.7)	22 (75.9)	0.22
A3: >40 years	9 (31.0)	5 (17.3)	
Location of the disease			
L1: ileal	11 (37.9)	9 (31.0)	
L2: colonic	1 (3.45)	2 (6.90)	0.78
L3: ileocolonic	17 (58.6)	18 (62.1)	
Disease behavior			
B1: inflammatory	13 (44.8)	8 (27.6)	
B2: stricturing	12 (41.4)	19 (65.5)	0.04
B3: penetrating	4 (13.8)	2 (6.90)	
Perianal disease, n (%)	11 (37.9)	13 (44.8)	1.0
Biologic therapy treatment, n (%)	17 (58.6)	20 (69.0)	0.53
Clinical disease activity, n (%)	9 (31.0)	11 (37.9)	0.46
Changes in CRP, n (%)	19 (65.5)	15 (57.7)	0.55

SD: standard deviation; CRP: C-reactive protein (mg/dL).

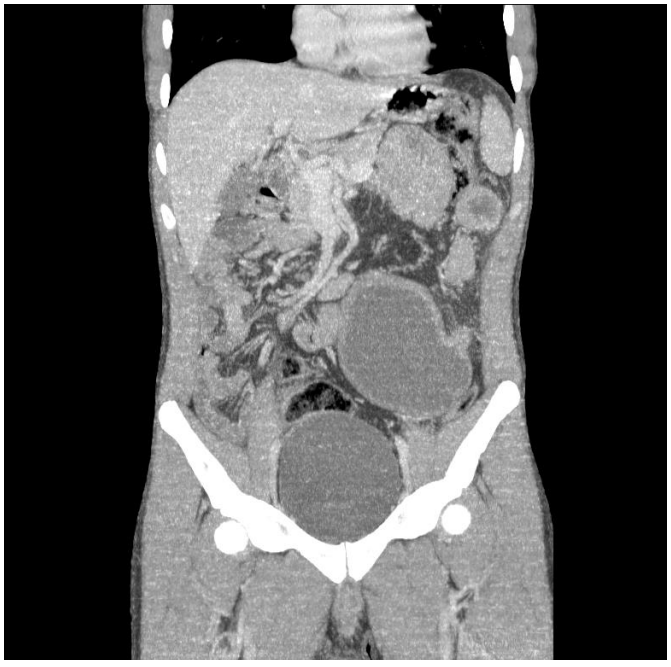

FIGURE 1. Male patient, 28 years old, presenting with jejunum Crohn's disease with stenosis and dilation of the small bowel, in the coronal.

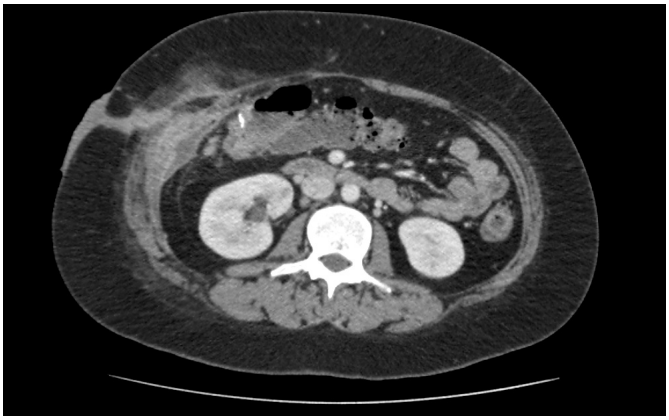

FIGURE 2. Female patient, 24 years old, presenting with ileocolonic Crohn's disease with enterocutaneous fistula.

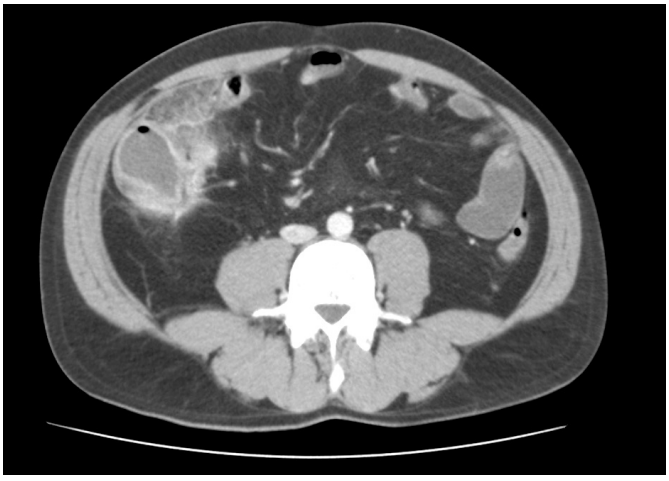

FIGURE 3. Male patient, 44 years old, presenting with ileocolonic Crohn's disease with an abscess in the ascending colon.

TABLE 2. Comparative analysis of the quality of the examination according to oral contrast agent volume.

	1,000 mL (n=29)	2,000 mL (n=29)	*P*
Adequate luminal filling, n (%)			
Jejunum	12 (41.4)	12 (41.4)	1.00
Ileum	23 (79.3)	24 (82.8)	0.83
Ascending colon	16 (55.2)	13 (44.8)	0.29
Transverse colon	9 (31.0)	12 (41.4)	0.64
Descending colon	9 (31.0)	6 (20.7)	0.46
Rectosigmoid	3 (10.4)	2 (6.89)	1.00
Number of filled segments, n (%)			
0	1 (3.45)	0 (0.00)	
1	5 (17.3)	11 (37.9)	
2	13 (44.8)	10 (34.5)	
3	4 (13.8)	4 (13.8)	0.58
4	4 (13.8)	2 (6.90)	
5	1 (3.45)	1 (3.45)	
6	1 (3.45)	1 (3.45)	
Adequate luminal distension, n (%)	7 (24.1)	9 (31.0)	0.45

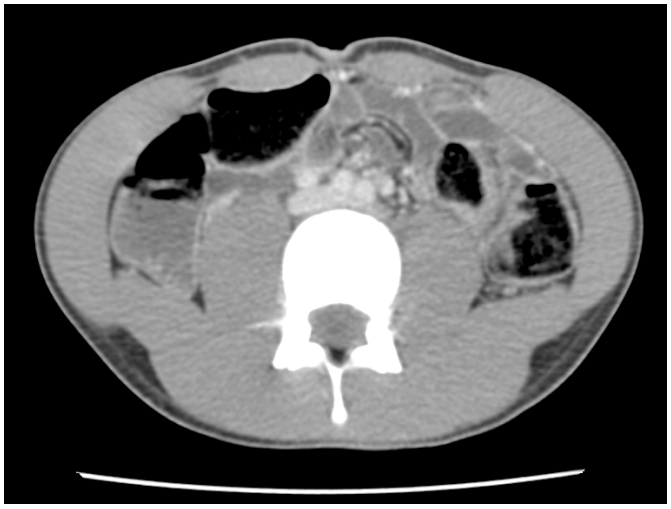

FIGURE 4. Male patient, 18 years old, ingestion of 1000 mL, with adequate intestinal filling.

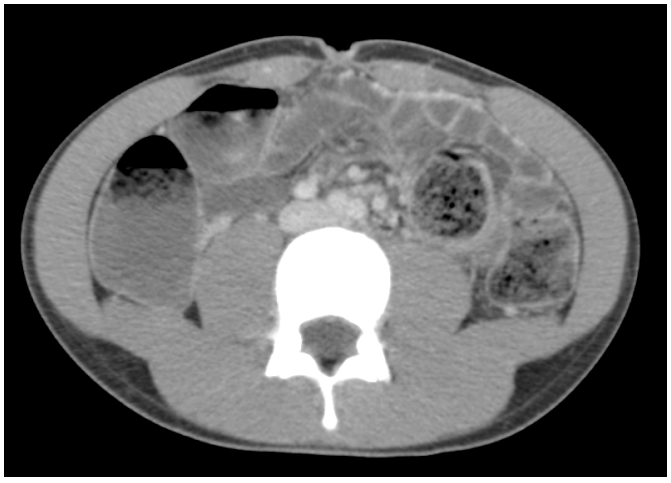

FIGURE 5. Male patient, 18 years old, ingestion of 2000 mL, with adequate intestinal filling.

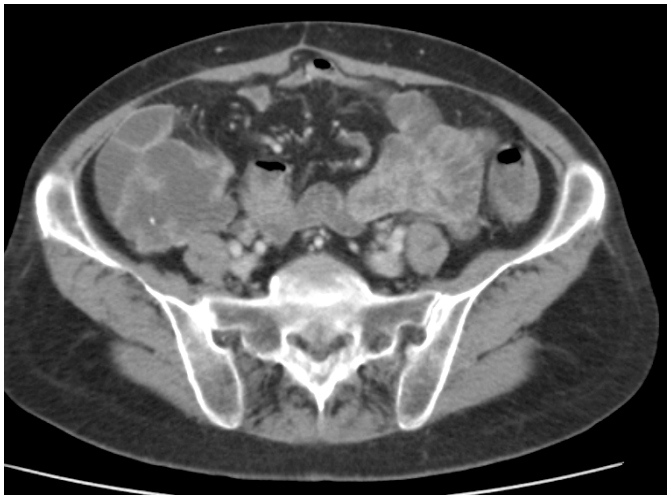

FIGURE 6. Female patient, 62 years old, ingestion of 2000 mL with good acceptance and adequate intestinal filling.

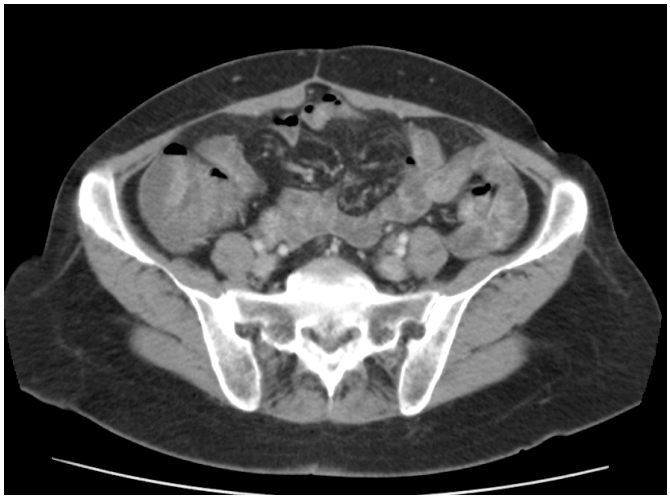

FIGURE 7. Female patient, 62 years old, ingestion of 1000 mL with the presence of nausea, and adequate intestinal filling.

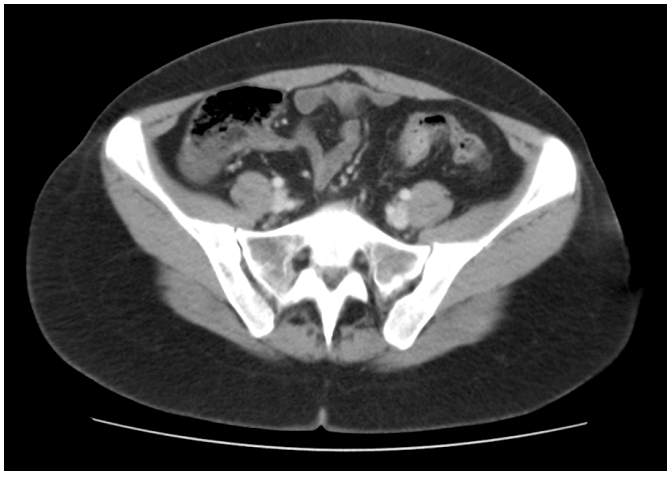

FIGURE 8. Male patient, 35 years old, ingestion of 1000 mL, presenting with ileocolonic Crohn's disease with fistula.

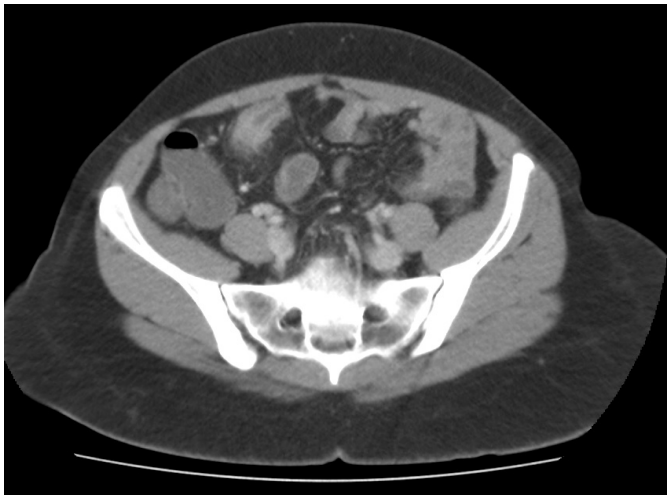

FIGURE 9. Female patient, 28 years old, ingestion of 2000 mL, presenting with ileocolonic Crohn's disease with stenosis.

the 2,000 mL group (*P*=0.06) (TABLE 3). The most commonly reported side effects were nausea (n=5), diarrhea (n=3), abdominal pain (n=2), and vomiting (n=1). FIGURE 1 shows that the two volumes of preparation identify the complications of the disease.

TABLE 3. Comparative analysis of acceptance and tolerance according to oral contrast agent volume.

	1,000 mL (n=29)	2,000 mL (n=29)	*P*
Easiness of ingestion, n (%)	19 (65.5)	11 (37.9)	0.07
Adequate taste, n (%)	12 (41.4)	15 (51.7)	0.30
Adequate time of ingestion, n (%)	21 (72.4)	17 (58.6)	0.22
Presence of side effect, n (%)	9 (31.0)	15 (51.7)	0.06

DISCUSSION

In recent years CT enterography has been widely used for the diagnosis and follow-up of CD due to its sensitivity in the detection of tissue inflammation, complications of the disease, structural changes and transmural scarring, which is a parameter for tissue response to clinical treatment[21,22,23].

The oral contrast agent used in CT enterography is considered to be an essential factor in the quality of the examination and, thus, for correct diagnosis of the disease and its complications. Inadequate preparation creates several problems, such as higher costs, exposure to radiation, distress to the patient, and the need for exam repetition[24,25].

A great variety of oral agents were used in CT enterography. Water is an acceptable agent for the proximal bowel. However, water is normally absorbed in the distal small bowel and becomes inefficient in the opacification and luminal distension of this segment. Thus, agents presenting higher osmotic pressure or that retain luminal fluid, such as methylcellulose, PEG, or sugar retainers, such as sorbitol and lactulose, are most appropriate for studying the bowel[9]. D'Ippolito et al.[10] compared three oral contrast agents (water, milk and PEG) and found the best bowel distension was obtained using PEG. However, this contrast agent was not tolerable due to the diarrhea presenting in 80% of assessed patients. Wong et al.[26] compared two commonly used oral agents in the United States: VoLumen and mannitol, and found that both provided adequate bowel distention and few side-effects. However, VoLumen is little used in our country and not often available. Zheng et al.[27] compared two oral preparations: mannitol and PEG and analyzed the quality, tolerance and acceptability of the preparations. In total, 70 patients were included, 35 in each group. Both preparations showed good intestinal distention and good visualization of the intestinal wall, however adverse events like nausea were more frequent in the PEG group.

Several studies describe good results for luminal filling and distension using contrast volumes ranging from 1,000 mL to 1,500 mL, regardless of the oral contrast agent used[28,29,30]. Few studies assessed volumes above 1,500 mL, which could provide better results regarding luminal filling and distension and improve diagnosis of CD complications. However, larger volumes promoted no improvement in distension and were more prone to provoking side effects such as nausea and vomiting, as observed in the present study.

In the present study the PEG contrast was efficient for the examination, regardless of the volume. There was no statistically significant difference between groups regarding segment filling, indicating that a larger volume does not necessarily imply more adequate filling. As for intestinal distension, only 16 patients obtained adequate distension regardless of volume. Barlow et al.[31] showed that inadequate distension can be caused by the incomplete ingestion of the contrast agent, a delay in the execution of the examination after ingestion of the contrast agent, retention of the contrast agent in the stomach or in the initial portion of the small bowel, or by rapid intestinal transit caused by disease activity. In the present study, the delay in the execution of the examination, and prolonged time of ingestion of the contrast, may have interfered with the quality of intestinal distension in some patients. More than 30% of patients who received 2,000 mL of the contrast agent exhibited difficulties ingesting the total volume due to discomfort caused by the large volume.

Side effects were more frequent in the 2,000 mL group, with no statistically significant difference (*P*=0.06). However, 31% of patients in the 1,000 mL group also exhibited side effects, which is a considerable amount considering the small volume of contrast agent. This can be explained by disease activity, confirmed by the presence of symptoms, changes in CRP values, and by the presence of disease complications, such as stenosis, dilations, and fistulas.

There are other methods prescribed for the diagnosis and follow-up of CD, including CT enteroclysis, capsule endoscopy, colonoscopy, conventional abdominal CT, and magnetic resonance enterography (MRE), with each presenting advantages and disadvantages. One advantage of capsule endoscopy is the analysis of the entire gastrointestinal tract. However, capsule is prohibited in cases of suspected intestinal obstruction[20]. CT enteroclysis promotes a more efficient intestinal distension, especially of the duodenum and jejunum. However, it is less accepted by patients owing to the need to pass an enteric tube for preparation[32]. Wold et al.[33] found no difference in the quality of intestinal distension promoted by CT enteroclysis and CT enterography. Siddiki et al.[34] compared MRE to CT enterography and found that both methods exhibited sensitivity regarding diagnosis of complications such as fistulas and abscesses. However, fistulas in the perianal region were better visualized with MRE[15].

The MRE is indicated to evaluate the complications of CD such as the presence of fistulas and identification of the fistulous pathway, presence of stenosis and differentiation between inflammatory stenosis versus fibrotic stenosis and has the advantage of the absence of radiation when compared to CT enterography[20,35] MRE is recommended in patients with inflammatory bowel disease, especially in those with Crohn's disease, due to the chronic nature of the disease and the frequent need to perform the exam. In the present study, the MRE was not the exam of choice due to the unavailability of the exam in the service and the high cost associated with the exam. The advantages of the CT enterography are the practicality of the exam and the lower cost, which is why it was the exam chosen for the evaluation of transmural complications of CD in this research.

There are some limitations to CT enterography in the diagnosis and follow-up of CD patients. First, small lesions of the intestinal mucosa, including exulcerations and ulcers, are usually not detected. Second, patients are submitted to ionizing radiation[36]. Indeed, most of these patients are young and many will have to repeat the examination several times during the course of treatment. Thus, it is important to limit the use of tomography in order to reduce radiation exposure. The care taken in the present study regarding a lower exposure to radiation included the use of modulated mA, a single phase of examination acquisition, and

good patient positioning and orientation. The arterial phase of CT enterography proved to be unnecessary[37]. If available, the use of MRE is recommended in these patients. It is important to note that the research led to the implementation of the Entero-TC protocol at the clinic hospital, further improving the care for patients with inflammatory bowel disease.

We concluded that the quality of CT enterography was not influenced by contrast volume. Despite this, there is no difference between acceptance and tolerance rates among contrast volume, but the 1,000 mL group exhibited a lower occurrence of side effects.

ACKNOWLEDGEMENTS

We thank Eloisa Elena Pascoalinotte from Botucatu Medical School at São Paulo State University (UNESP) for her valuable help in statistical analysis.

Authors' contribution

Renosto FL: performed the research. Barros JR: performed data collection from patients. Sassaki LY: revising it critically for important intellectual content and final approval of the version to be submitted. Bertoldi GA: analysis of data and reports. Marrone SR: analysis of data and reports. Saad-Hossne R: revising it critically for important intellectual content and final approval of the version to be submitted.

Orcid

Fernanda Lofiego Renosto: 0000-0002-2540-4920.
Jaqueline Ribeiro de Barros: 0000-0003-1451-8794.
Ligia Yukie Sassaki: 0000-0002-7319-8906.
Guilherme A Bertoldi: 0000-0002-4854-1020.
Sergio Ribeiro Marrone: 0000-0003-0732-2814.
Rogerio Saad Hossne: 0000-0002-8166-0304.

Renosto FL, Barros JR, Bertoldi GA, Marrone SR, Sassaki LY, Saad-Hossne R. Análise comparativa de dois volumes diferentes de agente de contraste oral para enterografia por tomografia computadorizada em pacientes com doença de Crohn. Arq Gastroenterol. 2021;58(3):322-8.

RESUMO – **Contexto** – A doença de Crohn (DC) é uma doença inflamatória intestinal caracterizada por uma inflamação crônica e recorrente do trato gastrointestinal causada por uma interação de fatores genéticos e ambientais. **Objetivo** – Comparar a qualidade e aceitação de dois volumes diferentes de contraste oral para enterografia por tomografia computadorizada em pacientes com doença de Crohn. **Métodos** – Um estudo transversal foi conduzido em 58 pacientes com doença de Crohn que receberam aleatoriamente um agente de contraste oral composto por 78,75 g de polietilenoglicol diluído em 1.000 mL ou 2.000 mL de água. Um exame foi realizado para avaliar a presença de inflamação ou complicações no intestino delgado. As variáveis incluíram a qualidade do preenchimento do segmento intestinal e distensão luminal e aceitação e tolerância do contraste oral nos pacientes. A análise estatística incluiu estatística descritiva e testes de associação. **Resultados** – Foram avaliados 58 pacientes, dos quais 58,6% eram mulheres, 34,5% apresentavam doença clinicamente ativa e 63,8% estavam recebendo terapia biológica. Quanto à análise comparativa entre os dois diferentes volumes de contraste oral, não foi encontrada diferença estatisticamente significativa em relação ao enchimento da alça intestinal (P=0,58) e distensão luminal adequada (P=0,45). Pacientes que receberam um volume maior (2.000 mL) exibiram efeitos colaterais com mais frequência (51,7% vs 31,0%; P=0,06) e tiveram maior dificuldade para ingerir o agente (65,5% vs 37,9%; P=0,07) em comparação com um volume de 1.000 mL. **Conclusão** – A qualidade da entero-tomografia computadorizada não foi influenciada pelo volume de contraste. No entanto, aceitação e tolerância foram melhores no grupo de 1.000 mL.

Palavras-chave – Agente de contraste; doença de Crohn's; polietilenoglicol; tomografia.

REFERENCES

1. Dignass A, Van Assche G, Lindsay JO, Lemann M, Soderholm J, Colombel JF, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Current management. J Crohns Colitis. 2010;4:28-62.
2. Gomollón F, Dignass A, Annese V, Tilg H, Assche GV, Lindsay JO, et al. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: part 1: diagnosis and medical management. J Crohns Colitis. 2017;11:3-25.
3. Bruining DH, Bhatnagar G, Rimola J, Taylor S, Zimmernann EM, Fletcher JG. CT and MR enterography in Crohn's disease: current and future applications. Abdom Imaging. 2015;40:965.
4. Anupindi SA, Grossman AB, Nimkin K, Mamula P, Gee MS. Imaging in the evaluation of the young patient with inflammatory bowel disease: what the gastroenterologist needs to know. JPGN. 2014;59:429-40.
5. Re Lo G, Cappello M, Tudisva C, Galia M, Randazzo C, Craxi A, et al. Ct enterography as a powerful tool for the evaluation of inflammatory activity in Crohn's disease: relationship of CT findings with CDAI and acute-phase reactants. Radiol. 2014;119:658-66.
6. Algin O, Metin MR, Karaoglanoglu M. Evaluation of enteroneovesical fistula by 64-detector CT enterography: A case report. Iran J Radiol. 2015;12:7349-55.
7. Minordi LM, Scaldaferri F, Marra RS, Pecere S, Larosa L, Poscia A, et al. Enterography CT without and with water enema in patients with Crohn's disease; Results from a comparative observational study in comparison with endoscopy. Eur J Radiol. 2016;85:404-13.
8. Baker ME, Hara AK, Platt JF, Maglinte DDT, Fletcher JG. CT enterography for Crohn's disease: optimal technique and imaging issues. Abdom Imaging. 2015;40:938-74.
9. Leduc F, De A, Rebello R, Muhn N, Ioannidis G. A comparative study of four oral contrast agents for small bowel distension with computed tomography enterography. Can Assoc Radiol J. 2015;66:140-4.
10. D'Ippolito G, Braga FA, Resende MC, Bretas EAS, Nunes TF, Rosas GQ, et al. Computed tomography enterography: a comparison of different neutral oral contrast agents. Radiol Bras. 2012;45:139-43.
11. Costa-Silva L, Martins T, Passos MCF. Enterografia por Tomografia Computadorizada: experiência inicial na avaliação das doenças do intestino delgado. Radiol Bras. 2010;43:303-08.
12. Al-Hawary MM, Kaza RK, Platt JF. CT Enterography: concepts and advances in Crohn's Disease imaging. Radiol Clin N Am. 2013;51:1-16.
13. Best WR, Becktel JM, Singleton JW, Jr-Kern F. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology. 1976;70:439-44.
14. Silverberg MS, Satsangi J, Ahmad T, Arnott IDR, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: Report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19:36-36.
15. Dambha F, Tanner J, Carroll N. Diagnostic imaging in Crohn's disease: What is the new gold standard? Best Pract Res Clin Gastroenterol. 2014;28:421-36.

16. Lopes S, Andrade P, Afonso J, Cunha R, Pinto RE, Ramos I, et al. Monitoring Crohn's disease activity: endoscopy, fecal markers and computed tomography enterography. Therap Adv Gastroenterol. 2018;11:1-12.
17. Macari M, Megibow AJ, Balthazar EJ. A pattern approach to the abnormal small bowel: observations at MDCT and CT Enterography. AJR. 2007;188:1344-55.
18. Cantarelli BC, Oliveira RS, Alves AM, Ribeiro BJ, Velloni F. D'ippolito G. Evaluating inflammatory activity in Crohn's disease by cross-sectional imaging techniques. Radiol Bras. 2020;531:38-46. DOI: 10.1590/0100-3984.2018.0096.
19. Furukawa A, Saotome T, Yamasaki M, Maeda K, Nitta N, Takahashi M, et al. Cross-sectional Imaging in Crohn Disease. Radiographics. 2004;24:689-702.
20. Bruining DH, Zimmermann EM, Loftus EV, Sandborn CG, Sauer CG, Strong SA, et al. Consensus recommendations for evaluation, interpretation, and utilization of computed tomography and magnetic resonance enterography in patients with small bowel Crohn's disease. Gastroenterology. 2018;154:1172-94.
21. Wu YW, Tang YH, Hao NX, Tang CY, Miao F. Crohn's disease: CT enterography manifestations before and after treatment. Eur J Radiol. 2012;81:52-59.
22. Bodily KD, Fletcher JG, Solem CA, Johnson CD, Fidler JL, Barlow JM, et al. Crohn Disease: mural attenuation and thickness at contrast-enhanced CT Enterography – correlation with endoscopic and histologic findings of inflammation. Radiology. 2006;238:505-16.
23. Minordi LM, Scaldaferri F, Larosa L, Marra R, Giordano F, Laterza L, et al. Comparison between clinical and radiological evaluation before and after medical therapy in patients with Crohn's disease: new prospective roles of CT enterography. Radiol Med. 2015;120:449-57.
24. Lee SS. Crohn Disease of the Small Bowel: comparison of CT Enterography, MR enterography, and small-bowel follow-through as diagnostic techniques. Radiology. 2009;251:751-61.
25. Baker ME. Mural Attenuation in Normal Small Bowel and Active Inflammatory Crohn's Disease on CT Enterography: Location, Absolute, Attenuation, Relative Attenuation and the Effect of Wall Thickness. AJR. 2009;192:417-23.
26. Wong J, Moore H, Roger M, Mckee C. CT enterography: mannitol versus VoLumen. J Med Imaging Radiat Oncol. 2016;60:593-8.
27. Zheng MQ, Zeng QS, Yu YQ, Ji R, Li YY, Zhang MM, et al. Evaluation of the performance of two neutral oral contrast agents in computed tomography enterography: A randomized controlled trial. J Dig Dis. 2020;21:112-9.
28. Afifi AH, Kassem MI. Crohn's disease: activity, complications and treatment. Evaluation using MDCT enterography and endoscopy. Egyptian Journal of Radiology and Nuclear Medicine. 2012;43:507-17.
29. Gaizo AJD, Fletcher JG, Yu L, Paden RG, Spencer GC, Leng S, et al. Reducing Radiation dose in Ct Enterography. Radiographics. 2013;33:1109-24.
30. Kolbe AB, Fletcher JG, Froemming AT, Sheedy SP, Koo CW, Pundi K, et al. Evaluation of patient tolerance and small-bowel distention with a new small-bowel distending agent for Enterography. AJR. 2016;206:994-1002.
31. Barlow JM, Goss BC, Hansel SL, Kolbe Ab, Rackham JL, Bruining DH, et al. CT enterography: technical and interpretive pitfalls. Abdom Imaging. 2015;40:1081-96.
32. Ghonge NP. CT enterography: state-of-the-art CT technique for small bowel imaging. Indian J Gastroenterol. 2013;32:152-62.
33. Wold PB, Fletcher JG, Johnson CD, Sandborn WJ. Assessment of small bowel Crohn Disease: noninvasive peroral CT enterography compared with other imaging methods and endoscopy: feasibility study. Radiology. 2003;229:275-81.
34. Siddiki HA, Fidler JL, Fletcher JG, Burton SS, Huprich JE, Hough DM, et al. Prospective Comparison of State-of-the-Art MR Enterography and CT Enterography in Small-bowel Crohn's disease. AJR Am J Roentgenol. 2009;193:113-21.
35. Takenaka K, Kitazume Y, Fujii T, Tsuchiya K, Watanabe M, Ohtsuka K. objective evalution for treat to target in Crohn's disease. J Gastroenterol. 2020;55:579-87.
36. Park MJ, Lim JS. Computed Tomography Enterography for Evaluation of Inflammatory Bowel Disease. Clin Endosc. 2013;46:327-36.
37. Kambadakone AR, Prakash P, Hahn PF, Sahani DV. Low-Dose CT Examinations in Crohn's Disease: Impact on Image Quality, Diagnostic Performance and Radiation Dose. AJR. 2010;195:78-88.